Amendments to the Specification

On page 4, please replace the paragraph starting on line 15 with the following:

Figure 1 shows the response of the interleukin-2 (IL-2) secreting mouse MHC class I dependent $CD8^+$ T cell hybridoma, B3Z [specific for the chicken ovalbumin "OVA" derived immunodominant peptide SIINFEKL (SEQ ID NO:22) (Jameson *et al.*, 1993, *J. Exp. Med.* 177: 1541)], to various antigens (Ag) presented by syngeneic superactivated dendritic cells (DC). CPM refers to counts per minute; Δcpm refers to a difference between the absolute cpm for a given test group minus the background cpm value obtained in the absence of the soluble Ag (in the experiment shown the latter was 9,581). The composition of the various antigens is indicated in the figure is described below.

On page 9, please replace the paragraph starting on line 34 with the following:

HER-2 peptide and polypeptide antigens can be isolated, synthesized or recombinantly expressed according to methods known in the art. The DNA coding sequence for HER-2/Neu/ErbB-2 may be found at sequence database GenBank™ Accession No. M11730 (human c-erb-B-2 mRNA).

On page 10, please replace the footnote with the following:

[1] 32 amino acids corresponding to amino acids 1 to 32 of ~~Genebank~~sequence database GenBank™ accession No.. NM_001099
[2] 3 amino acids corresponding to amino acids 33 to 35 of ~~Genebank~~sequence database GenBank™ accession No. NM_001099
[3] 3 amino acids corresponding to amino acids 19 to 21 of ~~Genebank~~sequence database GenBank™ accession No. M11730
[4] 289 amino acids corresponding to amino acids 22 to 310 of ~~Genebank~~sequence database GenBank™ accession No. M11730
[5] 217 amino acids corresponding to amino acids 1038 to 1254 of ~~Genebank~~sequence database GenBank™ accession No. M11730

On page 10, please replace the paragraph starting on line 13 with the following:

An immunostimulatory fusion protein construct of the invention may also include one or more sequence components selected from the group consisting of GM-CSF, a reporter sequence such as the imunodominant OVA-derived octapeptide SIINFEKL (SEQ ID NO:22) ($OVA_{257-264}$), one or more peptide signal sequences and a synthetic purification tag, *e.g.*, an added C-terminal amino acid sequence.

On page 11, please replace the paragraph starting on line 3 with the following:

Accordingly, the SIINFEKL (SEQ ID NO:22) ($OVA_{257-264}$) sequence, the PAP signal sequence, the mature PAP amino acid sequence, the HER-2 signal sequence, and the C-terminal peptide tag sequence set forth above are not necessary to generate such as response.

On page 11, please replace the paragraph starting on line 6 with the following:

The immunostimulatory fusion proteins of the invention may be modified by joining them, either covalently or noncovalently, with a reporter molecule. A wide variety of reporter molecules are known in the art and the selection of the reporter determines the assay format. For example, as detailed in Example 1, the OVA-derived imunodominant octapeptide SIINFEKL (SEQ ID NO:22) ($OVA_{257-264}$) was incorporated into exemplary immunostimulatory HER-2 fusion constructs and antigen presentation of the constructs evaluated. Briefly, the IL-2 secreting mouse T cell hybridoma B3Z, which responds to SIINFEKL (SEQ ID NO:22) ($OVA_{257-264}$), when bound to mouse MHC class I, was stimulated with DC that were pre-pulsed with the HER-2 fusion constructs, and the magnitude of response evaluated by measuring [^{3}H]thymidine incorporation in proliferating IL-2 dependent cells, as an indicator of antigen presentation.

On page 11, please replace the paragraph starting on line 16 with the following:

Additional examples of fusion proteins for use in practicing the invention include, but are not limited to those which include the sequence of a cancer antigen directly fused to the 217 amino acids of membrane distal intracellular HER-2 domain, without additional linker or signal peptide components. Examples of such fusion proteins include, but are not limited to: a fusion protein comprising 180 amino acids of the human autoimmunogenic cancer/testis antigen, NY-ESO-1 (amino acids 1 to 180 of sequence database GenBank™ Accession No. U87459), fused to the 217 amino acids of membrane distal intracellular HER-2 domain (amino acids 1038 to 1254 of sequence database GenBank™ Accession No. M 11730), presented herein as SEQ ID NO: 27, the coding sequence for which is presented as SEQ ID NO: 28); a fusion protein comprising 962 amino acids of the squamous cell carcinoma antigen, SART3-IC (amino acids 1 to 962 of sequence database GenBank™ Accession No. AB020880), fused to the 217 amino acids of membrane distal intracellular HER-2 domain (amino acids 1038 to

1254 of sequence database GenBank™ Accession No. M 11730), presented herein as SEQ ID NO: 29, the coding sequence for which is presented as SEQ ID NO: 30).

On page 12, please replace the footnote with the following:

[6]289 amino acids corresponding to amino acids 22 to 310 of ~~Genebank~~sequence database GenBank™ accession No. M11730.

On page 17, please replace the paragraph starting on line 4 with the following:

According to another aspect of the invention, DC's can be preserved by cryopreservation either before or after exposure to a HER-2 fusion protein of the invention. Exemplary methods for cryopreservation are further described in co-owned U.S. Ser. No. 60,168,991. For small scale cryopreservation, cells can be resuspended at 20-200.times.10^6 ml in precooled 5% human serum albumin (HAS) (Swiss Red Cross). An equal volume of 20% dimethylsulfoxide (DMSO) in the above HAS solution was then added dropwise. The mixture is aliquoted in cryovials at 1 ml/vial and frozen at -80°C in a cryochamber (available from the company Nalgene™) overnight. The vials are transferred to a liquid nitrogen tank in the morning. For large scale cryopreservation, cells can be resuspended at 30-600x10^6/ml in AIM V. An equal volume of 20% AIM V is then added gradually. The mixture is frozen in freezing containers (Cryocyte, Baxter) at 20 ml/bag using a rate-controlled freezing system (available from the company Forma™).

On page 17, please replace the paragraph starting on line 18 with the following:

An antigen presentation assay may be used to evaluate the antigen presenting ability of various immunostimulatory fusion proteins. An exemplary assay is described in Example 1, wherein the IL-2 secreting mouse T cell hybridoma B3Z, which responds to the mouse MHC class I (H2-K^b) bound OVA-derived peptide SIINFEKL (SEQ ID NO:22) ($OVA_{257-264}$; Jameson *et al.*, 1993, *J. Exp. Med.* 177: 1541), is stimulated with various DC that have been pre-pulsed with engineered HER-2 fusion proteins, and the magnitude of response is evaluated by measuring [^{3}H]thymidine incorporation in proliferating IL-2 dependent cells.

On page 23, please replace the paragraph starting on line 16 with the following:

Expression vectors comprising the coding sequence for various HER-2 fusion proteins were used to transfect mammalian 293-EBNA cells (available from the company Invitrogen™)

(transient expression) and insect SF21 cells (available from the company Clontech™, Palo Alto, CA). Fusion protein products were recovered from the tissue culture supernatants, and affinity purified by passage over a metal affinity column, (NTA resin, Qiagen). For HER500-hGM-CSF, analysis by SDS-PAGE revealed protein bands migrating at 120 kDa and 110 kDa as products from mammalian and insect cells, respectively. The predicted size of the 690 polypeptide backbone is 74877 kDa.

On page 23, please replace the paragraph starting on line 25 with the following:

The HER500*•rGM-CSF construct (SEQ ID NO: 4) was produced by expression of a coding sequence which included, in the 5' to 3' direction: a 32 amino acid PAP signal peptide, a 3 amino acid sequence of the mature PAP protein, an Ala Arg linker, a 3 amino acid HER-2 signal sequence, 289 amino acids of the mature HER-2 membrane distal extracellular domain, an Ala linker, the OVA-derived imunodominant octapeptide SIINFEKL (SEQ ID NO:22) ($OVA_{257-264}$), 217 amino acids of the HER-2 membrane distal intracellular domain, an Ala Ala linker, a 127 amino acid mature rat GM-CSF sequence, and Gly Ala Pro Pro Pro Pro Ala His His His His His His (SEQ ID NO:16).

On page 23, please replace the paragraph starting on line 33 with the following:

The HER300*•rGM-CSF construct (SEQ ID NO: 5) was produced by expression of a coding sequence which included, in the 5' to 3' direction: a 32 amino acid PAP signal sequence, a 3 amino acid sequence of the mature PAP protein, an Ala Arg linker, a 3 amino acid HER-2 signal sequence, 289 amino acids of the mature HER-2 membrane distal extracellular domain, an Ala linker, the OVA-derived imunodominant octapeptide SIINFEKL (SEQ ID NO:22) ($OVA_{257-264}$), an Ala linker, a 127 amino acid mature rat GM-CSF sequence, and Gly Ala Pro Pro Pro Pro Ala His His His His His His (SEQ ID NO:16).

On page 23, please replace the paragraph starting on line 40 with the following:

BP8 baculovirus expression vectors (available from the company Clontech™) comprising the coding sequence for the HER500*•rGM-CSF (SEQ ID NO: 9) or HER300*•rGM-CSF (SEQ ID NO: 10) fusion proteins were used to transfect SF21 cells. Fusion protein products were recovered from tissue culture supernatants, and affinity purified by metal affinity chromatography. Analysis by SDS-PAGE revealed protein bands migrating at 105 kDa for HER500*•rGM-CSF and 60 kDa for HER300*•rGM-CSF.

On page 24, please replace the paragraph starting on line 10 with the following:

The IL-2 secreting mouse T cell hybridoma B3Z, which responds to the mouse MHC class I (H2-K^b) bound OVA-derived peptide SIINFEKL (SEQ ID NO:22) ($OVA_{257-264}$; Jameson *et al.*, 1993, *J. Exp. Med.* 177: 1541), was used to evaluate the antigen presenting ability of HER-2 fusion proteins containing the OVA-derived immunodominant peptide SIINFEKL (SEQ ID NO:22).

On page 24, please replace the paragraph starting on line 14 with the following:

Tissue cultures were maintained in IMDM medium supplemented with 10% FCS, 2 mM L-glutamine, 0.1 mg/ml kanamycin sulfate and 3×10^{-5} M 2-ME (available from the company Gibco™, Grand Island, NY) at 37°C in a humidified atmosphere containing 5% CO_2 (tissue culture incubator).

On page 24, please replace the paragraph starting on line 27 with the following:

The response of B3Z cells to the HER300*•rGM-CSF and HER500*•rGM-CSF fusion proteins relative to OVA (Grade VII, 99% pure chicken ovalbumin purchased from the company Sigma™, St. Louis, MO), was evaluated *in vitro*. The cell proliferation response indicated as CPM based on 3H thymidine uptake (Fig. 1) indicate that HER300*•rGM-CSF and HER500*•rGM-CSF fusion proteins are more efficient in stimulating B3Z than native OVA itself (about, 10-fold, and >100-fold, respectively). The 10-fold superiority of HER500*•rGM-CSF over HER300*•rGM-CSF indicates that the enhanced presentation of Ag is correlated with the inclusion of the additional intracellular HER-2 domain derived 217 amino acids in the fusion protein (which are present in HER500*•rGM-CSF but absent in HER300*•rGM-CSF).

On page 26, please replace the paragraph starting on line 10 with the following:

While immunization with HER500*•rGM-CSF-pulsed DC prevented the tumor growth, treatment with HER300*•rGM-CSF had no effect (Fig. 2A). These results are consistent with the results obtained *in vitro* in that they confirm the importance of the intracellular HER-2 domain derived segment in attaining a strong level of Ag presentation in order to generate an effective anti-tumor response. Experimental results shown in Fig. 2B demonstrate that a significant level of *in vivo* protection against a HER-2 expressing tumor can also be generated (a) when HER500-containing immunogens are either fused to the human GM-CSF (HER500•hGM-CSF), (b) in the absence of any GM-CSF when both an intracellular and

extracellular portion of the HER-2 antigen is resent in the construct (HER500 and HER500*), and (c) in the absence of the OVA-derived peptide SIINFEKL (SEQ ID NO:22) (HER500 and HER500•hGM-CSF).